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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
PATTERSON, CHARLES L JR	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 08/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/031,496	ADNEY ET AL.	
	Examiner	Art Unit	
	Charles L. Patterson, Jr.	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 March 2004 and 21 June 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *14 January 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 because claim 12 refers to "asparagines 45, 270, or 384 of Table 4", but Table 4 contains 9 nucleotide sequences. There is no polypeptide sequence in Table 4 that contains "asparagines 45, 270, or 384". Because the examiner could examine the application without the sequence that contains these asparagines this was done, but the sequence must be supplied before the application is issued or claim 12 should be deleted or amended to not contain reference to these residues.

New 37 CFR 1.121(d) in 1272 OG 197 states:

> (d) Drawings. One or more application drawings shall be amended in the following manner: Any changes to an application drawing must be in compliance with Sec. 1.84 and must be submitted on a replacement sheet of drawings which shall be an attachment to the amendment document and, in the header, labeled "Replacement Sheet." Any replacement sheet of drawings shall include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is amended. All changes to the drawing(s) shall be explained, in detail, in either the drawing amendment or remarks section of the amendment paper.
>
> (1) A marked-up copy of any amended drawing figure, including annotations indicating the changes made, may be included. The marked-up copy must be clearly labeled as "Annotated Marked-up Drawings" and must be presented in the amendment or remarks section that explains the change to the drawings.
>
> (2) A marked-up copy of any amended drawing figure, including annotations indicating the changes made, must be provided when required by the examiner.

Applicants have submitted a corrected Figure 1 and 4 and have labeled the pages "IN THE FIGURES". These have not been entered as figures by the contractors processing the IFW as they are not labeled correctly and will therefore not appear as corrected figures in the issued application. Applicants should submit all figures per the rule quoted *supra*. As noted in the rule the final version of the figures should

not be marked up, although marked-up versions may be submitted. The figures submitted 3/8/04 are taken to be the marked-up version.

The disclosure is objected to because of the following informalities:

On page 5, lines 19-21, the recitation of "the sequence immediately upstream of the Not I site encodes a LysArg dipeptide" is not understood. The recitation is referring to Figure 3 and a Not I site does not appear in this figure.

Amended Figure 4 is objected to in that it states that "additional proline nucleotides" are shown. Proline is an amino acid, not a nucleotide and therefore this recitation is confusing and incorrect. Apparently applicants intended to recite "additional proline residues [or amino acids]" or else "additional nucleotides encoding proline".

Appropriate correction is required.

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-10 and 15-18 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. In U.S. patent practice there must be some indication of the intervention of "the hand of man" in a patent claim. These claims do not so indicate. Adding "isolated" or some similar recitation at the beginning of the claims would overcome this rejection.

Claims 1-18 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

The instant specification supposedly teaches variant exoglucanases having reduced glycosylation or that have an improvement in thermal tolerance. The instant claims are drawn to a nucleic acid that has a linker region of exoglucanase comprising a short sequence; a nucleic acid that encodes a variant cellobiohydrolase comprising a linker of 20-50 nucleotides that is between a catalytic domain and a binding domain; a method for making an active exoglucanase in a eukaryotic host comprising reducing glycosylation, wherein this reduced glycosylation is "replacing an N-glycosylation site amino acid residue with a non-glycosyl accepting amino acid residue"; three exoglycanases comprising short sequences and a combination of two of these sequences. The examiner has carefully read the instant specification and apparently what applicants have done is to disclose the various genetic manipulations in great detail but disclosed very little results or the utility of these manipulations. Table 1 discloses that when the CBHI from *Trichoderma reesei* is expressed in *Aspergillus awamori* with the three single site mutations and the two double site mutations shown in the table, the molecular weight is decreased somewhat. It is also shown that one of the mutations has enzymatic activity approximating the wild type enzyme. There is no proof shown that this decrease in molecular weight is advantageous. It is stated on page 6, last paragraph that the "rCBHI expressed in *A. awarmori* tends to be over glycosylated as evidenced by the higher molecular weight...[and] confirmed by digestion of the recombinant protein with endoglycosidases", but the disadvantage of this over glycosylation is not disclosed. The examiner admits that rCBHI N270A is shown to have activity in *A. awarmori*, but none of the claims

is limited to this embodiment. Neither is there stated in the specification a specific and substantial utility for this mutant having activity in *A. awarmori*. Claim 11 is drawn to making an active exoglucanase by reducing glycosylation of the enzyme by "replacing an N-glycosylation site amino acid residue with non-glycosyl accepting amino acid residue". It would have been obvious on its face that if a residue that can be glycosylated is replaced with one that cannot, the total glycosylation of the protein would be reduced.

Claim 1-18 also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claim 6-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 6 is confusing in the recitation of "comprising a linker region sequence...linker region". The recitation of "linker region" twice in the phrase is confusing.

Claims 7-10 are confusing and indefinite in the recitation of "claim 5", which claim has been cancelled. The claims are also indefinite in the recitation of "the variant cellobiohydrolase" of "the cellobiohydrolase", which terms do not have antecedent basis.

Claim 11 is confusing in the recitation of "replacing an N-glycosylation site amino acid residue with non-glycosyl accepting amino acid residue".

Apparently what applicants are trying to claim is that an amino acid that can be glycosylated is replaced with one that cannot be glycosylated, but the instant claim language does not clearly claim this. What is "an N-glycosylation site amino acid"? Is it one that has a N-glycosylation site or one which can undergo N-glycosylation? Changing the instant recitation to "replacing an amino acid residue that has an N-glycosylation site with one not having such a site" or some similar recitation would overcome this rejection.

Claims 12-14 are confusing in the recitation of "[t]he method[s]" of claim[s] 10". Claim 10 is not drawn to a method but rather to a nucleic acid. Apparently applicants intended to refer to claim 11, however "claims 10" in claim 13-14 and "methods" in claim 14 are confusing. Apparently "methods" and "claims" should be singular.

Claim 12 is indefinite in the recitation of "the N-glycosylation amino acid residues". There is no antecedent basis for this term in claim 10.

Claim 13 is incorrect in the recitation of "mutagenisis", which should apparently be "mutagenesis"

Claims 15-17 are confusing in the recitation of "comprising of the sequence". Apparently "of" should be deleted. The claims are also indefinite and confusing in the recitation of "sequence change of SEQ ID NO:20 [21, 22]". "Sequence change" implies that there was some starting sequence that was then changed, however the instant claim does not indicate what sequence was changed to the indicated sequences.

Claim 18 is confusing in the recitation of "claims 15,16", which recitation should apparently be "claims 15 and 16".

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-3 are rejected under 35 U.S.C. 102(b) as being anticipated by either of Nakari, et al. (A, B or N). The instant references teach SEQ ID NO:3 in SEQ ID NO:17 and Figure 16A, respectively. The other requirements of claims 2 and 3 are presumed to be inherently met since SEQ ID NO:3 is taught and the abstracts mention the *cbhI* gene, absent convincing proof to the contrary.

Claims 11-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Godbole, et al. (U). For the purpose of this rejection, claims 12-14 are presumed to depend upon claim 11. The instant reference teaches that when the *Trichoderma reesei cbh1* gene is transformed into *Pichia pastoris*, the rCBHI enzyme produced is overglycosylated and has less activity than the wild type CBHI enzyme produced by *Trichoderma reesei*. Since the enzyme is the same except for the glycosylation and the activity is increased, it would have been obvious to one of ordinary skill in the art that the decreased ac-

tivity in *Pichia pastoris* was due to the increased glycosylation and that decreasing the glycosylation would probably increase the activity of the enzyme. The presence of Asp 45, 270 and 384 is mentioned in column 1, page 833, second full paragraph. It would have therefore been obvious to one of ordinary skill in the art that if amino acids in the *cbh1* gene that can accept N-glycosylation were replaced with amino acids that cannot accept N-glycosylation, the activity would probably increase. There would have been at least a reasonable expectation of success and that is all that is required. The motivation would have been to increase the activity of the rCBHI enzyme in *Pichia pastoris*.

Claims 6 and 8 are rejected under 35 U.S.C. 102(b) as being anticipated by Srisodsuk, et al. (V). The instant reference teaches that CBH I has a catalytic domain linked by a 30-44 amino acid long linker domain to a cellulose domain. The term "variant cellobiohydrolase" is given no weight as the claim does not define what the enzyme is a variant of and because in evolution essentially all proteins are variants of some other protein.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Charles L. Patterson, Jr., PhD, whose telephone number is 571-272-0936. The examiner can normally be reached on Monday - Friday from 7:30 to 4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Charles L. Patterson, Jr.
Primary Examiner
Art Unit 1652

Patterson
August 18, 2004